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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,529	09/10/2003	Cary James Miller	215105.01500	5356

27160 7590 09/18/2008

KATTEN MUCHIN ROSENMAN LLP
(C/O PATENT ADMINISTRATOR)
2900 K STREET NW, SUITE 200
WASHINGTON, DC 20007-5118

EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
09/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,529	MILLER ET AL.	
	Examiner	Art Unit	
	MELANIE YU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-7,9-12,69 and 70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-7,9-12,69 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments and declaration submitted under 37 CFR 1.131 filed 21 May 2008 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 1, 2, 7, 9, 10, 12, 69 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang (US 6,670,115) in view of Oberhardt et al. (US 4,280,815) further in view of Piran et al. (US 6,087,088).

Zhang teaches an immunosensor system, comprising: a first immunosensor that includes a first immobilized antibody and generates a first signal (detection working electrode having an immobilized specific binding capture ligand, col. 3, lines 36-55; first signal is generated by a current produced by applying a potential between working and reference electrodes, col. 20, lines 33-39) based on a sandwich between the first

immobilized antibody, a target analyte and a labeled antibody (analyte is bound to the substrate through the first immobilized antibody, col. 3, lines 46-55 and label is attached to analyte, col. 4, lines 43-52), wherein a portion of the signal arises from non-specific binding of the labeled antibody in the region of the first immunosensor (although small, at least a portion of the first signal is due to non-specific binding, col. 28, line 40-col. 29, line 6); a second immunosensor (auxiliary electrode bound to the same substrate as the working electrode, col. 15, lines 3-6; auxiliary electrode, Fig. 7A) that generates a second signal that is compared to the first signal (potential applied between working electrode and auxiliary electrode to generate a second current signal that is compared to the potential applied between the working and reference electrodes that generates a first current signal, col. 20, lines 33-39 and col. 20, lines 27-44); and an analyzer configured to determine a corrected signal from the first and second signals (presence of analyte is determined by correlating the first and second signals, col. 18, line 35-col. 19, line 4). Zhang et al. fail to teach the second (auxiliary) electrode being a second immunosensor that includes a second immobilized antibody and acts as an immuno-reference sensor that generates a second signal that is predictably related to the degree of non-specific binding on the first immunosensor and also fail to specifically teach the immunoreactive compound being an endogenous or exogenous protein.

Oberhardt et al. teach a first immunosensor having a specific binding capture ligand for an analyte in a sample (antibodies, 14, are immobilized to an electrode, 10, and are specific for an antigen of interest, col. 6, lines 24-38; see Fig. 3a); a second immunosensor including a second immobilized antibody and acts as an immuno-

reference sensor and generates a second signal that is predictably related to the degree of non-specific binding which occurs in the region of the first immunosensor (second electrode, 11, has immobilized antibodies, 14a, that are not specific to the target antigens, and are therefore non-specific and antibodies are capture ligands, col. 6, lines 47-51; see Fig. 3a); and an analyzer configured to determine a corrected signal from the first and second signals (light signal from the second immunosensor is subtracted from light signal from the first immunosensor, col. 7, lines 1-24), in order to eliminate a washing step prior to detection of analyte.

Piran et al. teach an immunosensor system comprising: a first immunosensor that generates a signal based on the formation of a sandwich between an immobilized antibody, a target analyte and a labeled antibody, wherein a portion of the signal arises from non-specific binding of the labeled antibody in the region of the first immunosensor (antibody to the analyte is immobilized to the first immunosensor and the analyte and a labeled antibody form a complex, first antibody to analyte, col. 4, lines 27-30; target analyte bound with specific labeled probe, col. 5, lines 1-5; a label is specific for and binds to analyte, col. 5, lines 8-12; sandwich immunoassay, col. 6, lines 3-5; analyte TSH binds to immobilized anti-TSH and label binds to TSH, col. 6, lines 10-24); and a second antibody that generates a signal that is the same as the non-specific binding that occurs in the first immunosensor signal (second immunosensor is used as a reference and is used to adjust the signal of the first immunosensor for non-specific binding, reference signal mathematically corrects the signal from first labeled antibody, col. 4, lines 40-47), and has an immunocomplex between an immobilized antibody and

an endogenous or exogenous protein that is in the sample and is not the target analyte (antibody to IgG is immobilized on the second immunosensor and IgG is an endogenous or exogenous protein, anti-IgG is used for calibration purposes, col. 5, lines 59-67; col. 7, lines 44-67), wherein the antibody binds to a plasma protein, IgG, in order to increase sensitivity of a binding assay where analyte are present in low concentrations.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the system of Zhang, a second immunosensor having a non-specific binding capture ligand and correlating the signal from the second immunosensor with the signal from a first immunosensor as taught by Oberhardt et al., in order to provide a more accurate and precise assay. It would have further been obvious to one having ordinary skill in the art at the time the invention was made to include as the second antibody in the system of Yang et al., an antibody that binds nonspecifically to an exogenous or endogenous protein in a sample as taught by Piran et al., in order to provide an antibody that will produce an accurate signal of nonspecific binding and thus increases the sensitivity of the assay. Regarding claim 10, although Piran et al. do not specifically teach the binding affinity of the second antibody, the instant specification teaches that antibodies to analyte of IgG having an affinity constant within the required range of about 1x10(-7) to about 1x10(-15) at page 19, paragraph 85. As described above, Piran et al. teach an analyte of IgG and an antibody that binds to the analyte. Therefore according to the instant specification, the antibody to IgG has an affinity within the recited range.

With respect to claim 2, Zhang teaches the first and second immunosensor being electrochemical sensors (col. 4, line 66-col. 5, line 22).

Regarding claim 5, Zhang teaches the first and second immunosensor in a disposable cartridge (Fig. 8A-8B; col. 5, line 65 and col. 4, line 66-col. 5, line 12).

With respect to claim 6, Zhang teaches the target analyte being Troponin I (col. 13, lines 47-53 and col. 5, line 59-col. 6, line 4).

With respect to claims 9 and 12, the claims are drawn to the properties of a sample to be tested in the immunosensor system, the concentration of endogenous or exogenous protein in a sample and the type of sample. While the prior art does not specifically recite the concentration of protein in the sample as claimed, such a limitation is merely an intended use which the prior art would inherently be capable of doing. The only distinction between applicant's claims and the prior art is recited in the functional language. It is incumbent upon applicant to show that the application disclosed by Yang et al. is not actually capable of performing such functions. See *In re Ludtke 1971*, 169 USPQ 563 (CCPA 1971) and *In re Swinhartetal*, 169 USPQ 226 (CCPA 1971).

With respect to claims 69 and 70, Zhang teaches the sample being a blood sample (Fig. 8A and col. 8, line 66-col. 9, line 13).

3. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang (US 6,670,115) in view of Oberhardt et al. (US 4,280,815) further in view of Piran et al. (US 6,087,088), as applied to claim 1, and Pourmand et al. (US 2002/0155476).

Zhang in view of Oberhardt et al. further in view of Piran et al. teach first and second immunosensor including first and second immobilized antibodies, respectively,

but fail to teach the first and second immobilized antibodies immobilized on microparticles.

Pourmand et al. teach antibodies attached to an electrode through beads (par. 59, 70; antibodies, par. 54), in order to provide permanent attachment of molecules.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the immunosensor system of Zhang in view of Oberhardt et al. further in view of Piran et al., antibodies immobilized to the electrode through beads as taught by Pourmand et al., in order to provide convenient and simple attachment of molecules to an electrode. Pourmand et al. do not specifically teach first and second immobilized antibodies immobilized on beads, however it would have been obvious to one having ordinary skill to attach the antibodies of Yang et al. on beads and attach them to the appropriate electrode. Furthermore Pourmand et al. do not teach the specific size of the beads. However, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation" Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Since applicant has not disclosed that the specific limitations recited in instant claims 11 are for any particular purpose or solve any stated problem, and the

prior art teaches that the size of beads having immobilized antibodies may be varied depending on the desired electrode size and desired number of antibodies to be immobilized to the substrate, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures known in the microparticle art.

Response to Arguments

4. Applicant's arguments with respect to claims 1, 2, 5-7, 9-12, 69 and 70 have been considered and are persuasive but are moot in view of the new ground(s) of rejection. Applicant's declaration filed 21 May 2008 has been entered and is persuasive. The previous rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Zhang, which has an earlier filing date of 1999 and Oberhardt et al., which has a publication date of 1989 and teach the required limitations.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELANIE YU whose telephone number is (571)272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melanie Yu/
Patent Examiner, Art Unit 1641

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641